**UNITED STATES DISTRICT COURT**
**SOUTHERN DISTRICT OF WEST VIRGINIA**
**CHARLESTON DIVISION**

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| **IN RE: ETHICON, INC., PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION** | **Master File No. 2:12-MD-02327**<br>**MDL 2327**<br><br>**JOSEPH R. GOODWIN**<br>**U.S. DISTRICT JUDGE** |
| **THIS DOCUMENT RELATES TO:**<br>***Barbara & Gary Smith v Ethicon, Inc., et al***<br>***Case No. 2:12cv04791*** | |

# SUPPLEMENTAL EXPERT REPORT OF DOUGLAS H. GRIER, M.D.

**Supplemental review and opinion in the case of Barbara Smith, DOB 3/23/41**

I previously submitted a case-specific report regarding Barbara Smith. I incorporate that report by reference and stand by the opinions and bases set forth in those reports, as supplemented in this report. I also incorporate by reference in this report my general reports previously issued regarding the Prolift and TVT-O devices. I continue to hold the opinions set forth in my prior reports served in this case to a reasonable degree of medical certainty.

Since issuing my original case-specific report in this case, I have reviewed additional records—the most pertinent of which are summarized below. I have also continued to review the published literature regarding stress urinary incontinence and pelvic organ prolapse, and that literature further supports my opinions set forth in my earlier reports, as discussed below.

**Supplemental medical summary (in addition to visits documented in my first report)**

On 4/9/10, Ms. Smith was noted to be doing well except for sexual dysfunction that was thought to be possibly related to her high-dose Zoloft. She was diagnosed with sexual functioning problems associated with high-dose Zoloft on 5/13/10.

Ms. Smith saw Dr. Peter Zenthoefer on 7/8/11 and was noted to have vaginal mesh erosion near the vaginal apex, which was not successfully treated with vaginal estrogen cream.

On 7/18/2011, Ms. Smith was seen by Carlene Pompei, LPN for her voiding trial. Her bladder was filled by Foley with 275 ml, the Foley was removed, and Ms. Smith voided 250 ml without difficulty. At her post-op follow up with Dr. Zenthoefer on 7/26/2011, her incisions were “ok” and stitches were intact. She was to use vaginal Estrogen cream.

Ms. Smith was treated for a UTI on 5/7/12 with Trimethoprim. Her urine culture grew >100,000 Klebsiella pneumoniae and >100,000 Escherichia coli. On 5/21/2012, she was prescribed Cephalexin for a urine culture that grew >100,000 Klebsiella pneumoniae.

On 6/1/2012, she was seen for bilateral hip injections and reported she felt like her UTI symptoms were coming back. She was prescribed Macrodantin and Premarin. Her urinalysis showed 1+ hemoglobin, 0-5 WBCs, 0-3 bacteria, and few epithelial cells.

On 6/6/2012, she was seen by Dr. Ritter for vaginal irritation x 3 days since starting estrogen cream. By exam, scant mucous with suture visible in the anterior and superior aspect. She was to follow up with GYN. On 6/10/2012, she presented to the ER with suprapubic pain x 2 weeks. There were no findings to suggest an acute infection. She was referred to GYN. Her mesh exposure continued through June 2011 and was instructed to use Estrogen vaginal cream. Her urine culture on 6/11/2012 showed no growth.

On 6/16/2012, she was referred to the ER for urinary retention. She was found to have suprapubic pain, urinary retention, hypotension and dysuria for more than a week. No pelvic exam was performed. She was given Rocephin and prescribed Augmentin to treat a UTI and

referred to urology. Her urine culture grew urine culture grew multiple organisms, indicating probable contamination or colonization not related to infection.

On 6/25/2012, she was seen in the ER again for dark, malodorous discharge from either the urethra or vagina for 12-24 hours. By exam, there was a light brown vaginal discharge in the vault that was sent for culture. She was prescribed Keflex for a UTI and instructed to follow up with OB/Gyn and probable endometrial biopsy. Her vaginal cultures were negative. Her urine culture grew approximately 10,000 Escherichia coli.

On 6/28/2012, she returned to the ER for vaginal discharge and bladder infection x 1 month. Her exam showed visible mesh at 12 o'clock 2/3rd up the vagina. She was prescribed topical steroid cream for periurethral inflammation. It was noted her last positive urine culture was 5/21/2012. She was referred to Dr. Clark for possible rectovaginal fistula work-up.

On 7/3/2012, she was seen by Dr. Sean Clark where her exam showed poorly estrogenic thin vaginal mucosa, a small cystocele, and vaginal mesh palpable in the proximal anterior vagina with about 1.5 cm segment exposed. An in-office cystoscopy showed a very thin mucosa covering blue-green visible mesh or suture material at the distal trigone. The recommendation was for conservative treatment for UTI with fluids, probiotics, clean intermittent catheterization twice daily, and to follow up with urogynecology about vaginal mesh erosion.

On 7/10/2012, Ms. Smith presented to Dr. Amanda Clark where she reported "poop" coming from her vagina for several days. The vaginal mesh erosion was unchanged. Her rectal exam showed mesh palpable inside the rectovaginal septum. She was prescribed Augmentin. She followed up on 7/17/2012 where a CT of pelvis showed a 3 cm pocket at the top of the vaginal cuff. No further drainage and opening no longer present at top of vagina. She was to complete antibiotic course.

On 7/30/2012, she was seen by Dr. Amanda Clark where her pain and discharge were resolved but she reported dysuria. She was prescribed Clindamycin. She was to undergo an excision of abscess and involved mesh with possible removal of entire mesh.

On 8/16/2012, Ms. Smith underwent a diagnostic laparoscopy, cystoscopy with placement of ureteral catheters, exploratory laparotomy with lysis of adhesions, abdominal drainage of pelvic abscess, vaginal excision of mesh, cystourethroscopy performed by Dr. Amanda Clark. Her pre-op diagnosis was pelvic abscess at the vaginal cuff, mesh erosion x 2. Her post-op diagnosis was the same plus small bowel adhesions. Dr. Clark noted in her findings: "…Exam confirmed the two areas of mesh erosion noted anteriorly slightly larger, 4 x 1 cm, elliptical in shape, posterior 2 x 5 mm, both involving the mid vaginal walls and not involving the apex. No evidence of vaginal drainage or discharge…" Dr. Clark documented the operative report "…The anterior mesh was addressed first. It should be noted that on bimanual palpation from abdominal and vaginal, there was no communication noted between the vagina and peritoneal cavity. The cephalad end of the mesh erosion anteriorly came to the region of the abscess location, but no communication was noted. The mesh was grasped with a tonsil placed on tension…The mesh

was then identified and a piece approximately 1 cm in size was dissected. When dissecting cephalad toward the abscess cavity, the mesh abruptly ended consistent with the prior mesh removal. After excision of the mesh, there was no remaining exposed mesh other than that incorporated into surrounding tissue…The posterior mesh was grasped and managed similarly. A 1.5 x 1 cm piece of mesh was removed." There were no complications. The pathology report for "vaginal mesh" consisted of two flattened portions of tan synthetic material consistent with mesh which are 1.0 and 17 cm in greatest dimension. Ms. Smith was discharged to home on 8/21/2012.

On 8/30/2012, Ms. Smith was seen by Dr. Amanda Clark for her post-op follow up. She reported urge incontinence and urgency worse at night. Her vaginal incisions were healing. Her bladder scan was 9 ml residual urine volume. She was to restart Estrogen-Premarin. Her urinalysis showed leukocytes 2+, nitrite positive, protein 1+, hemoglobin 3+. Her urine culture grew >100,000 Enterobacter cloacae. She was prescribed Macrobid for a UTI. On 9/4/2012, her antibiotic was changed to Doxycycline.

On 9/27/2012, Ms. Smith was seen by Dr. Clark where she reported nocturia x 3, urge incontinence at night, and often wakes with a wet pad. She reports improvement after prescription for UTI. Her exam showed no evidence of mesh erosion, one Polysorb suture present accounting for discharge that was wiped away, and palpable mesh but not tender vaginally. She was prescribed Ditropan XL and to return as needed.

A 12/3/2012 urine culture grew > 100,000 Escherichia coli and >100,000 Klebsiella oxytoca. On 12/4/2012, Ms. smith was informed of results by telephone and was prescribed Macrobid.

On 1/15/2013, Ms. Smith called and spoke with Joan Gaul, RN. She reported urinary urgency, some frequency. Ms. Smith reported she stopped the Ditropan "it did not work." Her urine culture grew >100,000 Klebsiella oxytoca. She was seen by Dr. Rahel Nardos on 1/16/2013. Her urinalysis showed 2+ esterase, nitrite positive, bacteria >20, WBC > 40, and RBC 0-3. She was prescribed Macrobid. Through January 2013, Ms. Smith continued to complain of UTI symptoms with negative urinalysis.

On 2/11/2013 and 2/14/2013 her urinalysis tests were negative for leukocytes and nitrites. On 5/3/2013, she was seen by Dr. Clark for complaints of urinary frequency and burning with urination. She was prescribed Macrobid. Her urine culture grew > 100,000 Enterococcus species. In July 2013 she was treated for a UTI with Macrobid. Her urine culture grew >100,000 Escherichia coli.

On 3/25/2014, Ms. Smith was seen by Dr. Clark for right lower quadrant pain, concerned for adhesions. Her pain was described as burning pain for 2 weeks. It was noted she had 2 UTIs in the last four months. By exam, there was no mesh erosion or suture seen. She could consider PT if symptoms do not improve on their own. On 4/10/2014, Ms. Smith called to report dysuria, frequent and painful urination x 3 weeks. A urinalysis was noted not consistent with a UTI and may be due to vaginal atrophy. She was advised to use Estrogen.

On 11/2/15, Ms. Smith presented with a complaint of vaginal irritation. It was noted that she had throbbing vaginal pain. She noted it initially resolved with estrogen cream. She described her pain as being located at the urethral opening. Exam revealed her external genitalia were red and irritated with areas of fissuring. The vagina had noted atrophy and moderate slightly thick whitish discharge.

On 10/29/2015, Ms. Smith was seen by Karista Bradley, RN for dysuria. Her urine culture grew >100,000 Escherichia coli. It was documented that Ms. Smith was called with results and antibiotics were ordered.

On 11/2/2015, Ms. Smith was seen by Vivian S. Liu, NP for vaginal irritation. On exam, vaginal atrophy and moderate slightly thick whitish discharge was noted. She was prescribed Diflucan and Nystatin/Triamcinolone Ointment.

She was seen by Dr. Ritter on 4/11/2016 for left lower quadrant abdominal pain found to be muscular. She was to have labs and CT to rule out infection. If benign, she would be referred for physical therapy for muscular cause.

On 5/12/2016, she was seen by Michelle Marie Cerruti, LPN for dysuria, burning/painful urination, frequency, urgency and low pelvic pain. Her urine culture grew >100,000 Escherichia coli. Antibiotics were ordered per Dr. Ryan.

On 7/6/16, in a visit with Dr. Michelle Ritter at Kaiser Permanente, it was noted that Ms. Smith had fecal incontinence and a lot of diarrhea for more than 6 months.

In a 10/21/2016 telephone encounter, it was noted she was treated for Macrobid to treat a UTI. Her urine culture grew >100,000 Escherichia coli.

On 2/2/2017, she was treated for a UTI by phone with Macrodantin. Her urinalysis grew >100,000 Escherichia coli. Multiple urine drug screens in 2017 show the use of Morphine, Oxycodone, and Oxymorphone.

**Supplemental Opinions**

Recent published literature regarding mid-urethral slings such as the TVT-O and transvaginal mesh grafts such as the Prolift device support my opinions regarding the safety and efficacy of those devices. The literature shows that the devices were not defective.

A recent study by Gurol-Urganci and colleagues observed that the rate of re-operation after mid-urethral sling surgery was 6.9% at 9 years.[1] A study published in 2019 showed a 2.4% rate

[1] Gurol-Urganci, et al., Long-term Rate of Mesh Sling Removal Following Midurethral Mesh Sling Insertion Among Women With Stress Urinary Incontinence. JAMA. 2018;320(16):1659-69.

of revision procedures following mid-urethral sling implantation.[2] A registry study involving 38,500 women showed a significantly higher rate of re-operation after the Burch procedure than after the TVT procedure.[3]

In 2019, Clancy and colleagues published a case-control study noting that the risk of having a mid-urethral sling revision procedure was only 2.4% for women receiving a mid-urethral sling between 2005 to 2016.[4] The 2017 Ford Cochrane Review supports the safety of full-length mid-urethral slings like the TVT-O. It notes that Type I mesh like the mesh in the TVT-O device "has the highest biocompatibility with the least propensity for infection." It notes that "macroporous meshes (pore size in excess of 75 µm) easily allow macrophages, leukocytes, fibroblasts, blood vessels and collagen to transverse the pores: thus macroporous meshes promote tissue host ingrowth with resultant biocompatibility and low risk of infection (Amid 1997). Monofilament tapes are widely available and now predominate in current clinical practice."[5]

Serati published the 10-year results of a TVT-O study and showed there were no vaginal, bladder, or urethral erosions. No patients underwent resection of the mesh during the 10-year follow-up period, and 97% of the patients declared themselves cured. 92% were objectively cured.[6] Fusco's 2017 systematic review studied 28 randomized controlled trials involving nearly 16,000 patients, and found that women who received mid-urethral slings had significantly higher overall cure rates than patients receiving a Burch colposuspension. The risk of vaginal mesh erosion was 2.8% with trans-obturator slings, which was lower than the rate with outside-in trans-obturator slings. Trans-obturator slings like the TVT-O had a reduced incidence of intra-operative bladder or vaginal perforation, UTIs, hematoma, and voiding lower urinary tract symptoms.[7]

Additionally, AUGS & SUFU updated their position statement on mesh mid-urethral slings in February 2018, again noting that the polypropylene material in mid-urethral slings is safe and effective as a surgical implant and has been used extensively—in millions of patients around the world.[8] The 2017 AUA/SUFU guidelines regarding the surgical treatment of SUI in women note that there is Grade A evidence supporting offering index patients who opt for mid-urethral sling

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[2] Clancy AA, et al., Predictors of sling revision after mid-urethral sling procedures: a case-control study. BJOG. 2019 Feb;126(3):419-26.

[3] Kurkijärvi K, et al., Reoperations for Female Stress Urinary Incontinence: A Finnish National Register Study. Eur Urol Focus. 2018 Sep;4(5):754-59.

[4] Clancy AA, et al., Predictors of sling revision after mid-urethral sling procedures: a case-control study. BJOG. 2019 Feb;126(3):419-26.

[5] Ford AA, et al., Mid-urethral sling operations for stress urinary incontinence in women. Cochrane Database Syst Rev. 2017 Jul 31;7:CD006375.

[6] Serati M, et al., Tension-free Vaginal Tape-Obturator for Treatment of Pure Urodynamic Stress Urinary Incontinence: Efficacy and Adverse Effects at 10-year Follow-up. Eur Urol. 2017 Apr;71(4):674-79.

[7] Fusco F, et al., Updated Systematic Review and Meta-analysis of the Comparative Data on Colposuspensions, Pubovaginal slings, and Midurethral tapes in the Surgical Treatment of Female Stress Urinary Incontinence. Eur Urol. 2017 Oct;72(4):567-91.

[8] AUGS & SUFU Position Statement, Mesh Midurethral Slings for Stress Urinary Incontinence (updated Feb. 2018).

surgery either a retropubic or a trans-obturator mid-urethral sling. The guidelines support the safety of mid-urethral slings and note that OAB symptoms and dyspareunia can occur after any pelvic surgery.[9]

In the retrospective study by Luo and colleagues referenced above, none of the patients followed for an average of 8 years abstained from sexual intercourse due to the Prolift or Prosima operation or post-operative discomfort, and all reported that they would have the procedure again and would recommend it.[10] In the Ubertazzi 5-year retrospective cohort study, there was a 79.2% cure rate and only 5.5% of the patients had to undergo another operation for prolapse recurrence. There was an approximate 16% rate of mesh exposure and an approximate 13% rate of de novo dyspareunia.[11]

The 5-year follow-up results from the OPTIMAL randomized controlled trial were published in 2018, and they show that suture exposures and granulation tissue also occur with non-mesh native tissue repairs such as uterosacral ligament suspensions and sacrospinous ligament fixation surgeries. The data also shows significant failure rates for those procedures—61% (USLS) and 70% (SSLF).[12] This supports my opinion that Ms. Smith's Prolift device was a more durable treatment option for her prolapse than native tissue repairs were.

Ms. Smith was noted to have a 3-cm pocket at the top of the vaginal cuff on 7/10/12, and had an abdominal drainage of the pelvic abscess on 8/16/12 with lysis of adhesions and excision of anterior and posterior mesh exposures. The infection that Ms. Smith experienced is not indicative of a defect in the Prolift mesh. It is made of macroporous, Type I mesh—Gynemesh PS—which has 2.5 mm pores, which are well in excess of the threshold pore size (>75 µm) to allow for macrophages to clear any bacteria that may be present. Infections can occur in connection with any pelvic surgery—whether mesh is utilized as a graft material or not—and the fact that she experienced a pelvic abscess is not indicative of a defect in the Prolift device. Lysis of adhesions was necessary in the 8/16/12 surgery, and her adhesions are another likely cause of her pain.[13] With respect to Ms. Smith's UTIs, it is also possible that fecal incontinence is contributing to those.

Dr. Elliott's 5/23/19 supplemental report notes that Ms. Smith was not able to make a fully informed decision regarding the implantation of Prolift mesh because he contends that Ethicon failed to fully disclose the risks of the Prolift device in the IFU for the device. In my opinion, the

[9] Kobashi KC, et al., Surgical Treatment of Female Stress Urinary Incontinence: AUA/SUFU Guideline. J Urol. 2017 Oct;198(4):875-883.

[10] Luo DY, et al., Long term Follow-up of Transvaginal Anatomical Implant of Mesh in Pelvic organ prolapse. Sci Rep 2018;8(2829).

[11] Ubertazzi EP, et al., Long-term outcomes of transvaginal mesh (TVM) In patients with pelvic organ prolapse: A 5-year follow-up. Eur J Obstet & Gynecol and Reprod Biol. 2018;225:90-94.

[12] Jelovsek JE, et al., Effect of Uterosacral Ligament Suspension vs Sacrospinous Ligament Fixation With or Without Perioperative Behavioral Therapy for Pelvic Organ Vaginal Prolapse on Surgical Outcomes and Prolapse Symptoms at 5 Years in the OPTIMAL Randomized Clinical Trial. JAMA. 2018;319(15):1554-65.

[13] Lower AM, et al., Adhesion-related readmissions following gynaecological laparoscopy or laparotomy in Scotland: an epidemiological study of 24046 patients. Human Reprod. 2004;19(8):1877-1885.

IFU for the Prolift device was appropriate and allowed surgeons to use the device safely for its intended purposes. Any prolapse procedure—whether utilizing mesh, native tissue, or another graft material—can result in chronic vaginal pain and dyspareunia, continued incontinence, or other voiding problems.[14] These facts are commonly known among pelvic floor surgeons, as are the facts that mesh that acts as a scaffold for the incorporation of tissue could cause partner dyspareunia in the event of an exposure, or could be difficult to remove in toto. It is not necessary for the IFUs for these products to advise pelvic floor surgeons of the possibility of chronic vaginal pain, dyspareunia, partner dyspareunia, and the inability to remove the entire mesh.

None of Ms. Smith's alleged injuries were caused by defects in the Prolift or TVT-O devices.

I hereby incorporate by reference my general reports regarding the Prolift and TVT-O products submitted in this litigation, as well as my original case-specific report in this case.

**Dated:** 6/22/19

Douglas H. Grier, M.D.

[14] Kobashi KC, et al., Surgical Treatment of Female Stress Urinary Incontinence: AUA/SUFU Guideline. J Urol. 2017 Jun 15 ("All surgical interventions (MUS, PVS, colposuspension) to treat SUI have potential adverse outcomes, such as continued incontinence, voiding dysfunction, urinary retention, pain, and dyspareunia.").